

**REMARKS**

Applicant has carefully studied the nonfinal Examiner's Action mailed July 16, 2004 and all references cited therein. The amendment appearing above and these explanatory remarks are believed to be fully responsive to the Action. Accordingly, this important patent application is now believed to be in condition for allowance.

**Anticipation under 35 U.S.C. §102(B)**

Claims 1 and 2 stand rejected under 35 U.S.C. §102(B) as anticipated by Sawada (Electrophoresis, 20, 1999, 24-30). Applicant believes this rejection is moot since Sawada neither recites Applicants column, as amended, comprising a sol-gel coating or a deactivation agent.

It is well settled that Under 35 U.S.C. §102, anticipation requires that each and every element of the claimed invention be disclosed in the prior art.<sup>1</sup> Sawada, does not teach, describe, or suggest a sol-gel process to create a stationary phase coating bound to a capillary inner surface. Therefore, the present invention, as amended in claim 1, cannot be said to be anticipated by the reference. Furthermore, since claim 2 depends from claim 1 (which has been shown to be patentable over the prior art) and thereby contains all limitations set forth therein, claim 2 cannot be anticipated by Sawada as a matter of law.

Accordingly, withdrawal of the rejection on these grounds, as well as a notice of allowance, is solicited.

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<sup>1</sup> *Akzo N.V. v. U.S. International Trade Commission*, 1 USPQ 2d 1241, 1245 (Fed. Cir. 1986), *cert. denied*, 482 U.S. 909 (1987); See also, *W.L. Gore & Associates v. Garlock, Inc.*, 220 USPQ 303, 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984) (Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration.); *Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co.*, 221 USPQ 481, 485 (Fed. Cir. 1984) (Anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, *arranged as in the claim.*) (emphasis added); *Scripps Clinic & Research Foundation v. Genentech Inc.*, 18 USPQ 2d 1001, 1010 (Fed. Cir. 1991) (Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. . . . There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention.)

**Obviousness under 35 U.S.C. §103(a)**

Applicant acknowledges the recitation of 35 U.S.C. §103(a)

***Sawada***

Claims 1 and 2 stand rejected under 35 U.S.C. §103(a) as being obvious over Sawada (Electrophoresis, 20, 1999, pages 24-30). The Office asserts that if a difference exists between the claims and Sawada, it would reside in optimizing the elements of Sawada. As a motivation for the "optimization" of these elements, the Office cites the motivation to enhance separation.<sup>2</sup>

To establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art.<sup>3</sup> Moreover, all words in a claim must be considered in judging the patentability of that claim against the prior art.<sup>4</sup> Since Sawada does not include all the limitations of claim 1 as amended (a sol-gel stationary phase), it cannot render the obvious as a matter of law. Also, since claim 2 depends from claim 1, which has been shown to be patentable over the prior art by virtue of the amendments listed above and these remarks, is also nonobvious.<sup>5</sup>

Accordingly, withdrawal of the rejection on these grounds, as well as a notice of allowance, is solicited.

***Guo in view of Snyder and Zhang***

1. *The proposed modification changes the principle of operation of the prior art.*

Claims 1-9 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Guo (Anal. Chem. 1995, 67, 2511-2516) in view of Snyder (Introduction to Modern Liquid Chromatography, pp 2780289), and Zhang (Journal of Liquid Chromatography, 18(17), 2273-3396 (1995)).<sup>6</sup>

Applicant respectfully submits that the Office has not met its burden of establishing a *prima facie* case of obviousness. The proposed modification would change the principle of operation of the prior art, thus the references are insufficient to render claim 1 *prima facie* obvious.<sup>7</sup>

<sup>2</sup> Office Action, mailed July 16, 2004, pg 2

<sup>3</sup> *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)

<sup>4</sup> *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970)

<sup>5</sup> MPEP §2143.03, citing *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)

<sup>6</sup> Office Action, pg 2.

<sup>7</sup> MPEP §2143.01, pg 2100-132

Citing *In re Ratti*, the MPEP establishes that were a suggested combination of references would require a substantial reconstruction and redesign of the elements shown in the references as well as a change in the basic principle under which the referenced construction was designed to operate, the reference(s) cannot serve to support a *prima facie* case of obviousness.<sup>8</sup>

Here, the Office has cited Guo as the primary reference. The present invention differs from Guo not only with respect to surface charge but also with respect to electro-osmotic flow (EOF), the mechanism by which a mobile flows through the column. In the approach used by Guo, the direction of the mobile phase through the column is from the anode to the cathode (cathodic EOF). This movement is generated by the residual negative (-) charge created by the dissociation of surface silanol groups. In contrast, the present invention provides an elegant means of generating anodic EOF (reversed EOF, from cathode to anode). This ability to control the magnitude of EOF in the column is missing from the prior art.

In Guo, the EOF in the CEC columns becomes inoperable under low pH conditions (~2-3) due to the protonation of the surface silanol groups. The present invention, however, provides a reliable means to sustain a strong EOF (hence mobile phase flow through the column) over a wide pH range.

Similarly, Zhang employs octadecyldimethyl(propylsilyl) ammonium groups in high-performance liquid chromatography (HPLC) where mechanical pumps are used to drive the mobile phase through the column. The positive charge in the stationary phase improves the chromatographic separation (which was acknowledged by the office in the Office Action<sup>9</sup>). The positive (+) surface charge plays no role in processes associated with mobile phase flow. In the present invention the direction of the mobile phase flow is reversed through the use of a positively-charged sol-gel stationary phase thereby providing a strong EOF through the column over a wide pH. The modification proposed by the Office is a significant departure from the basic principle under which Zhang was designed to operate and cannot be used to find obviousness.<sup>10</sup>

Accordingly, withdrawal of the rejection on these grounds, as well as a notice of allowance, is solicited.

<sup>8</sup> *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)

<sup>9</sup> "substituting octadecyldimethyl(propylsilyl) ammonium groups for C<sub>18</sub> leads to unique chromatographic selectivity" Office Action, pg 3.

<sup>10</sup> See *In re Ratti*

2. *The prior art does not contain a suggestion or motivation to modify the references.*

The Office asserts as the motivation to combine the references that Zhang discloses substituting octadecyldimethyl(propylsilyl) ammonium groups for C<sub>18</sub> leads to unique chromatographic selectivity; and a fair reading of Snyder indicates that the C<sub>8</sub> compounds (Guo) and C<sub>18</sub> compounds (Zhang) are in the same family of reversed phase compounds. As discussed *supra*, however, the instant invention uses a positively-charged sol-gel stationary phase, through the use of a quaternary amine group in the precursor providing a positive surface charge, thereby providing a strong EOF through the column over a wide pH. The octadecyl ligand in the surface coating provides chromatographic interaction with the analytes. Since the surface charge discussed in Zhang has no effect associated with mobile phase flow, it cannot be used as a motivation to combine Zhang and Guo, regardless of Snyder, to achieve the present invention.

None of the references cited speak to using a charged surface to control direction of the mobile phase through the column. The level of skill in the art, established by Snyder, cannot be relied upon to provide a suggestion to combine references simply because they *can be* combined.<sup>11</sup> Since the references do not speak to such use, they cannot logically suggest a combination to achieve such a use. Accordingly, the first element of a *prima facie* case of obviousness<sup>12</sup> has not been met.<sup>13</sup>

3. *The prior art does not contain all the claimed limitations.*

None of the references cited by the Office teach, describe, or suggest the use of a deactivation reagent in the sol-gel stationary phase. Column deactivation refers to chemical derivatization of the silanol groups that can offer adsorptive interactions with the solute molecules (especially the polar ones). Deactivation is very important to achieve high column efficiency and to avoid peak tailing. The method described in the prior for the preparation of the monolithic column makes no attempt to deactivate the column, and for good reasons. In the monolithic columns of the prior art, silanol groups serve as the source of the surface charge to generate EOF which is essential for the operation of the columns in CEC. Chemical

<sup>11</sup> MPEP §2143.01, citing *Al-site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999)

<sup>12</sup> MPEP §2143

derivatization of the silanol groups, however, will reduce the surface charge, and consequently, decrease the EOF in the column. This will lead to an increase in analysis time. The prior art uses bare silica particles to increase the silanol contents in the column, and hence, to increase EOF. At the same time, the use of bare silica in the monolith renders the column prone to undergoing deleterious adsorptive interactions with polar analytes hurting the column performance.

The present invention does integrate a deactivation process in the column preparation method. To this end, a deactivating reagent, such as phenyldimethylsilane (PheDMS) was incorporated in the sol solution. Unlike the prior art, a reduction of the column silanol content does not lead to a decrease in the EOF in the sol-gel monolithic columns described in the present invention providing reversed EOF due to the presence of positively charged quaternary amine groups. Deactivation leads to increased EOF in the sol-gel monolithic columns of the present invention. Thus, in the sol-gel monolithic columns of the present invention, deactivation provides two significant advantages: (a) high column efficiency by reducing the deleterious adsorptive interactions with the solute molecules and (b) fast EOF in the column.

As previously discussed, to establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art.<sup>14</sup> Moreover, all words in a claim must be considered in judging the patentability of that claim against the prior art.<sup>15</sup> Since none of the references include all the limitations of claim 1 as amended (a sol gel stationary phase comprising a deactivation agent), they cannot render the claim obvious as a matter of law. Also, since claims 2 through 9 depend from claim 1, which has been shown to be patentable over the prior art by virtue of the amendments listed above and these remarks, they are also nonobvious.<sup>16</sup>

***Guo in view of Snyder, Zhang and in further view of Frechet***

Claims 3-9 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Guo in view of Snyder and Zhang (as applied to claims 1-9) and in further view of Frechet.

Applicant respectfully traverses this rejection on the grounds stated above which have shown claim 1 to be nonobvious, and hence patentable, over the prior art. Claims 3 through 9

<sup>13</sup> See *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998) (The combination of the references taught every element of the claimed invention, however without a motivation to combine, a rejection based on a *prima facie* case of obviousness was held improper).

<sup>14</sup> *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)

<sup>15</sup> *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970)

depend, either directly or indirectly, from claim 1. If an independent claim is shown to be nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious as a matter of law.<sup>17</sup>

### *Conclusion*

Applicant agrees that the art made of record and not relied upon is not more pertinent to the invention than the art cited as a reference against the claims.

Entry of a Notice of Allowance is solicited. If the Office is not fully persuaded as to the merits of Applicant's position, or if an Examiner's Amendment would place the pending claims in condition for allowance, a telephone call to the undersigned at (727) 507-8558 is requested.

Very respectfully,

SMITH & HOPEN

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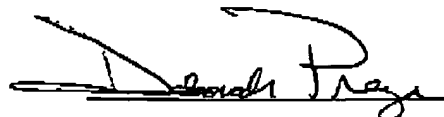
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### CERTIFICATE OF FACSIMILE TRANSMISSION

(37 C.F.R. 1.8 (a))

I HEREBY CERTIFY that this Amendment A, including Amendments to the Claims, and Remarks, is being transmitted by facsimile to the United States Patent and Trademark Office, Art Unit 1723, Attn: Ernest G. Therkorn, (703) 872-9310 on January 17, 2005.

Dated: January 17, 2005



Deborah Preza

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<sup>16</sup> MPEP §2143.03, citing *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)

<sup>17</sup> *Id.*